REMARKS

I. Status Summary

Claims 23-30 and 32-46 are pending in the present application. All rejections and objections presented in the previous Official Action have been withdrawn.

Claims 23-30 and 32-46 have been rejected under the written description requirement of 35 U.S.C. § 112, first paragraph.

Claims 23, 27, 28, 30, 32, 33, 34, 37-40, and 43-46 have been rejected under 35 U.S.C. § 102(e) upon the contention that they are anticipated by U.S. Patent Application Publication No. 2002/0168351 of Ohno (hereinafter "Ohno").

Claims 23, 25, 27, 28, 30, 32, 33, 34, 36-40, and 43-46 under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Ohno in view of PCT International Patent Application Publication No. WO 97/41210 of Nair *et al.* (hereinafter "Nair"). Claims 23-25, 27, 28, 30, 32, 33, 34, and 36-46 have also been rejected under this section upon the contention that they are unpatentable over Ohno and Nair and further in view of U.S. Patent No. 6,077,519 to Storkus *et al.* (hereinafter "the '519 Patent"). Claims 23, 27, 28, 30, 32, 33, 34, 37-40, and 43-46 have also been rejected under this section upon the contention that they are unpatentable over Ohno.

Claims 23 and 33 have been amended. The amendments replace the term "derived" with "obtained". Support for the amendments can be found throughout the specification as filed, including particularly on page 1, first paragraph ("proteins and/or peptides which are overexpressed in tumor cells or which are derived from tumor cells"; emphasis added) in view of priority document WO 02/074338 at page 1, first paragraph ("Proteine und/oder Peptide codieren, die in Tumorzellen überexprimiert werden oder die aus Tumorzellen stammen"; emphasis added), in which the German word "stammen", which can be translated as "originates from", has been translated as "derived from". Additional support can be found on page 2, first paragraph ("Activated T lymphocytes recognize ligands consisting of peptides derived from a protein expressed in tumor cells..."); at page 5, second paragraph ("proteins and/or peptides which are overexpressed in tumor cells or are derived from autologous tumor cells or from several different tumor cell lines"); and at pages 5-6, bridging paragraph ("RNA derived from autologous tumor cells is reverse transcribed"). In each of these instances, the phrase "derived from" is being employed in the context of "isolated from", "originates from", or "obtained from", BASED ON THE German language priority document, and not in the context of being modified from any such biomolecule.

Accordingly, applicants respectfully submit that no new matter has been introduced by the amendments to the claims.

Reconsideration of the application as amended and in view of the remarks set forth herein is respectfully requested.

II. Response to the Written Description Rejection

Claims 23-30 and 32-46 have been rejected under the written description requirement of 35 U.S.C. § 112, first paragraph. According to the Patent Office,

> The specification fails to provide a definition for "derived from" which would limit the proteins and/or peptides to those which are obtained from autologous tumor cells without modification. Thus, when given the broadest reasonable interpretation, proteins and/or peptides derived from autologous tumor cells include modified proteins or peptides having structural alterations. The specification describes only proteins or peptides obtained from tumor cells without modification. Thus, the specification fails to adequately describe proteins or peptides which are "derived from" tumor cells and thus comprise structural alterations. One of skill n the art would reasonable conclude that applicant was not in possession of the claimed genus of derivatized proteins or peptides obtained from tumor cells.

Non-Final Official Action at page 2.

Applicants respectfully disagree. Applicants respectfully submit that the proper approach to examining claim terms under the written description requirement of 35 U.S.C. § 112, first paragraph, it set forth in M.P.E.P. § 2163, which states in part: "Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description" (emphasis added). Similarly, M.P.E.P. § 2111 states:

> During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." The Federal Circuit's en banc decision in *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005) expressly recognized that the USPTO employs the "broadest reasonable interpretation" standard:
>
> > The Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set

> forth in the remainder of the specification
> and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR 1.75(d)(1).

As such, applicants respectfully submit that the claim terms must be construed in a manner that is consistent with the specification, and any interpretation that is not consistent with the specification is believed to be improper. For example, applicants respectfully submit that the Patent Office's assertion that "the specification fails to adequately describe proteins or peptides which are 'derived from' tumor cells and thus comprise structural alterations" actually supports applicants' contention that this is not the meaning that the phrase at issue is intended to have.

To elaborate, applicants respectfully submit that the phrase "derived from" is being employed in the specification as synonymous with "isolated from" or "originating from". This meaning is also consistent with the German term "stammen" as employed in the priority document: PCT International Patent Application Publication No. 02/074338. Applicants respectfully submit that the German term "stammen" means "comes, derives, or originates from". Thus, applicants respectfully submit that after review of the instant specification, one of ordinary skill in the art would understand that the phrase at issue is intended to mean that the "proteins and/or peptides or RNA or DNA or cDNA encoding said proteins and/or peptides which are... derived from autologous tumor cells" are properly construed to be proteins and/or peptides or RNA or DNA or cDNA encoding said proteins and/or peptides which are obtained from autologous tumor cells.

Nonetheless, in an effort to facilitate prosecution, applicants have amended the phrase "derived from" in claims 23 and 33 to "obtained from". Support for the amendments can be found throughout the specification as filed, including particularly on page 1, first paragraph in view of priority document WO 02/074338 at page 1, first paragraph. Additional support can be found on page 2, first paragraph; at page 5, second paragraph; and at pages 5-6, bridging paragraph. Accordingly, applicants respectfully submit that no new matter has been introduced by the amendments to the claims.

Summarily, applicants respectfully submit that claims 23 and 33 have been amended to clarify a context for the term "derived from" that the Patent Office concedes on page 2 of the Non-Final Official Action is described in the specification. Therefore, applicants

respectfully submit that the instant rejection is believed to have been addressed, and applicants respectfully request that it be withdrawn at this time.

III. Response to the Anticipation Rejection

Claims 23, 27, 28, 30, 32, 33, 34, 37-40, and 43-46 have been rejected under 35 U.S.C. § 102(e) upon the contention that they are anticipated by U.S. Patent Application Publication No. 2002/0168351 of Ohno (hereinafter "Ohno"). According to the Patent Office, Ohno teaches a method for treating cancer comprising the administration of chimeric cells comprising tumor cells fused to autologous dendritic cells. The Patent Office asserts that with respect to claims 28, 34; 43 and 44, Ohno recites a list of cancers that can be treated using the chimeric cells comprising tumor cells fused to autologous dendritic cells. Furthermore, the Patent Office asserts that (a) with respect to claims 45 and 46, Ohno discloses that CTL in the patient receiving the fusions cells is stimulated by the presentation of mucin antigens or Her-2/neu epitopes; (b) with respect to claim 37, Ohno discloses intravenous, subcutaneous and intramuscular routes of administration of the fusion cells; (c) Ohno meets the limitations of claims requiring RNA from tumor cells which has been introduced in recombinant form because the expression of the tumor cell peptides by the fused dendritic cell is a recombinant form of expression of the tumor cell RNA; and (d) it would be inherent in the fusion cells of Ohno that proteins or peptides which are over expressed in the tumor cells would be expressed by the dendritic cell fusion via the over expressed RNA present in the tumor cell of the fusion.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants respectfully submit that the Patent Office has misinterpreted the meaning of the term "HLA-haploidentical" as used in the instant specification. Particularly, applicants respectfully submit that "autologous" and "HLA-haploidentical" are mutually exclusive.

To elaborate, applicants respectfully submit that autologous cells are HLA-identical: they are identical at every HLA locus since the donor and the recipient are the same individual. This is set forth in more detail on pages 8-11 of the AMENDMENT IN RESPONSE TO NON-FINAL OFFICE ACTION submitted May 29, 2007. As set forth therein, an autologous cell, which is "HLA-matched" or "HLA-identical" is not the equivalent of an "HLA-haploidentical". Page 8 of the May 29, 2007 Amendment states:

> [i]n order for antigen-presenting cells to be HLA-haploidentical to those of a patient, the donor of the antigen-presenting cells and the patient must be related and must have both inherited the same HLA gene complex on one of their copies of chromosome 6, but not of their other copy of chromosome 6. As a result, all of the alleles of the HLA gene complex on one of the two copies of chromosome 6 of the HLA-haploidentical antigen-presenting cell will generally be identical to those of the patient.

May 29, 2007 Amendment at page 8 (emphases added). Therefore, applicants respectfully submit that as used in the instant application, the phrase "HLA-haploidentical" in fact excludes "autologous" since autologous antigen-presenting cells would not be characterized by genetic identity in only one of the two copies of the chromosome 6 HLA complex.

Stated another way, independent claims 23, 27, and 33 all recite *inter alia* that the antigen-presenting cells (APCs) are HLA-haploidentical with respect to those of the patient. Thus, HLA-haploidentical cells are not believed to be HLA-identical cells.

Since Ohno is asserted to disclose the use of autologous APCs, applicants respectfully submit that Ohno does not support a rejection of claims 23, 27, and 33 under 35 U.S.C. § 102(e). Claims 28, 30, 32, 34, 37-40, and 43-46 all depend directly or indirectly from claim 23, 27, or 33, and thus are also believed to be distinguished over the cited reference. Accordingly, applicants respectfully request that the instant rejection of claims 23, 27, 28, 30, 32, 33, 34, 37-40, and 43-46 under 35 U.S.C. § 102(e) over Ohno be withdrawn at this time.

IV. Responses to the Obviousness Rejections

Claims 23, 25, 27, 28, 30, 32, 33, 34, 36-40, and 43-46 under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Ohno in view of Nair. Claims 23-25, 27, 28, 30, 32, 33, 34, and 36-46 have also been rejected under this section upon the contention that they are unpatentable over Ohno and Nair and further in view of the '519 Patent. Claims 23, 27, 28, 30, 32, 33, 34, 37-40, and 43-46 have also been rejected under this section upon the contention that they are unpatentable over Ohno.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

IV.A. Response to the Rejection over Ohno *in view of* Nair

Claims 23, 25, 27, 28, 30, 32, 33, 34, 36-40, and 43-46 under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Ohno in view of Nair. According to the Patent Office, Ohno teaches fusions of autologous dendritic cells with tumor cells for the expression of the tumor cell peptides by the dendritic cell. the Patent Office concedes, however, that Ohno does not teach autologous dendritic cells which are transfected with nucleic acids encoding tumor cell peptides to produce the expression of said peptides by the autologous dendritic cells. According to the Patent Office, this deficiency is cured by Nair, which is asserted to teach a method for the loading of dendritic cells by introduction of a tumor associated RNA which is unfractionated or cDNA made by PCR. The Patent Office further asserts that Nair discloses: (a) that the method offers advantages in that there is no need to identify specific tumor rejection antigens and an immune response to unfractionated RNA or cDNA made therefrom elicits immune responses to several tumor antigens reducing the likelihood of escape mutants and extends the use of active immunotherapy to the treatment of cancers for which specific tumor antigens have not yet been identified which is the vast majority of cancers; and (b) a method for treating cancer comprising directly administering the loaded dendritic cells to a patient suffering from cancer. From this, the Patent Office contends that it would have been *prima facie* obvious to substitute the RNA or cDNA-transfected dendritic cells to a patient having cancer.

Applicants respectfully submit that the combination of Ohno and Nair does not support a rejection under 35 U.S.C. § 103(a). Particularly, applicants respectfully submit that even assuming *arguendo* that the Patent Office's characterization of the Nair reference is correct, the Patent Office's interpretation of the Ohno reference is inaccurate as set forth hereinabove with respect to the rejection under 35 U.S.C. § 102(e), and the Nair reference does not cure this deficiency.

To elaborate, applicants respectfully submit that Ohno does not disclose or suggest employing HLA-haploidentical APCs. Applicants respectfully submit that every reference to APCs in Ohno discloses the APCs to be autologous. Given that autologous cells are not HLA-haploidentical, applicants respectfully submit that Ohno cannot be read to disclose or suggest using HLA-haploidentical APCs as recited in the instant claims.

Applicants respectfully submit that Nair does not cure this particular deficiency. Therefore, even assuming *arguendo* that one of ordinary skill in the art would have considered administering RNA- or cDNA-transfected dendritic cells into a patient having

cancer, the combination of Ohno and Nair would have led one of ordinary skill in the art at best to administer RNA- or cDNA-transfected autologous dendritic cells. Applicants respectfully submit that this is not the subject matter of the instant claims, and thus the combination of Ohno and Nair fails to support a rejection of claims 23, 25, 27, 28, 30, 32, 33, 34, 36-40, and 43-46 under 35 U.S.C. § 103(a).

Accordingly, applicants respectfully submit that the Patent Office has not presented a *prima facie* case of obviousness of claims 23, 25, 27, 28, 30, 32, 33, 34, 36-40, and 43-46 under 35 U.S.C. § 103(a) over the combination of Ohno and Nair. As such, applicants respectfully request that the instant rejection be withdrawn at this time.

IV.B. Response to the Rejection over Ohno *in view of* Nair *and further in view of the '519 Patent*

Claims 23-25, 27, 28, 30, 32, 33, 34, and 36-46 have also been rejected under 35 U.S.C. § 103(a) upon the contention that they are unpatentable over Ohno and Nair and further in view of the '519 Patent. According to the Patent Office, the combination of Ohno and Nair render obvious the instant invention regarding the loading of haploidentical APCs with unfractionated RNA or cDNA made therefrom from tumor tissue from the patient. The Patent Office concedes that the combination does not teach or suggest the use of multiple tumor cell lines as a source of peptides, RNA or cDNA for loading or pulsing dendritic cells. The Patent Office contends, however, that the '519 Patent teaches that dendritic cells can be pulsed with HLA-attached allogeneic tumor cell lines as an alternative to acid eluted peptides from the patients tumor cells; the administration of pulsed dendritic cells by intravenous routes; and that the invention can be applied to treat colon, squamous, gastric, breast, prostate, lung, cervical and ovarian carcinomas. From this, the Patent Office asserts that it would have been *prima facie* obvious to use pooled tumor cell acid eluted peptides or RNA or cDNA for pulsing or loading the dendritic cells used in the methods rendered obvious by the combination of Ohno and Nair.

Applicants respectfully disagree. Initially, applicants respectfully submit that as set forth hereinabove, the combination of Ohno and Nair does not render obvious the instant invention regarding the loading of HLA-haploidentical APCs with unfractionated RNA or cDNA made therefrom from tumor tissue from the patient. Applicants respectfully submit that there is no disclosure in either Ohno or Nair that teaches or suggests the use of HLA-haploidentical APCs.

Applicants further respectfully submit that the '519 Patent does not cure this deficiency. Review of the '519 Patent suggests that the '519 Patent contemplates pulsing autologous dendritic cells with HLA-attached allogeneic tumor cell lines as an alternative to acid eluted peptides from the patients tumor cells. The Patent Office's attention is directed to col. 1, lines 25-27 ("the present invention further relates to use of autologous dendritic cells pulsed with acid-eluted peptides..."); col. 5, lines 28-30 ("Still yet another object of the present invention is to provide autologous dendritic cell and acid stripped peptide-based vaccines for treatment of cancer patients"); col. 5, lines 31-35 (vaccines based on "tumor peptides pulsed onto autologous bone marrow-or peripheral blood-derived dendritic cells"); Figures 18 and 19 (anti-melanoma CTL using autologous DCs pulsed with melanoma peptides); col. 12, lines 21-23 ("Another aspect of the present invention is the use of acid-eluted peptides/T cell epitopes from a patient's tumor cells that are pulsed onto autologous dendritic cells to treat that particular patient"); col. 32, lines 9-12 ("autologous/sygeneic DC loaded with acid-eluted tumor peptides can drive cellular immune responses in vitro and in vivo, leading to the suppression of growth or eradication of established tumors"; note that "syngeneic" animals are genetically identical, so they are HLA-identical and not HLA-haploidentical); col. 35, lines 46-48 ("autologous/syngeneic DC pulsed with acid-eluted peptides derived from syngeneic tumors markedly inhibited or erradicated tumor progression in mice bearing tumors"); col. 41, lines 9-12 ("DC can be generated from a patient's blood rather than from their bone marrow"; use of the patient's own autologous DCs); Example 25; and the Abstract ("autologous dendritic cells as the basis for antitumor vaccines") (emphases added in each case).

In summary, it is believed that every instance in which an APC is disclosed in the '519 Patent to be manipulated to express a tumor antigen, the APCs are disclosed as being autologous to the patient into which they are or would be administered. Therefore, applicants respectfully submit that like Ohno, the '519 Patent discloses the use of autologous APCs, and cannot be read to suggest the use of HLA-haploidentical APCs. As a result, applicants respectfully submit that the '519 Patent does not cure the deficiency of Ohno or Ohno and Nair with respect to the use of HLA-haploidentical APCs.

Accordingly, applicants respectfully submit that the combination of Ohno, Nair, and the '519 Patent fails to support a rejection of claims 23-25, 27, 28, 30, 32, 33, 34, and 36-46 under 35 U.S.C. § 103(a). Therefore, applicants respectfully request that the instant rejection be withdrawn at this time.

IV.C. Response to the Rejection over Ohno

Claims 23, 27, 28, 30, 32-34, 37-40, and 43-46 have been rejected under 35 U.S.C. § 103(a) upon the contention that they are unpatentable over Ohno. According to the Patent Office, Ohno teaches using antigen-presenting cells which are autologous. Ohno does not teach dendritic cells from haploidentical individuals. The Patent Office asserts, however, that it would have been *prima facie* obvious to use a mixture of haploidentical dendritic cells and autologous dendritic cells in the event that there was a deficiency in the quantity of dendritic cells obtained from the patient. The Patent Office further contends that one of skill in the art would have been motivated to provide more dendritic cells in place of the autologous dendritic cells in order to obtain enough of the dendritic cell-tumor cell chimeric cells with which to treat the patient.

Applicants respectfully disagree. Initially, applicants respectfully submit that Ohno does not disclose or suggest the use of HLA-haploidentical APCs. Applicants respectfully submit that Ohno is directed entirely towards employing autologous APCs, which as set forth in more detail hereinabove, are not believed to be HLA-haploidentical. Therefore, applicants respectfully submit that the Patent Office has not provided a *prima facie* case of obviousness of claims 23, 27, 28, 30, 32-34, 37-40, and 43-46 over Ohno.

Additionally, M.P.E.P. § 2142 cites the decision in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007) of the Court of Appeals for the Federal Circuit (hereinafter the "Federal Circuit") for the proposition that "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness' (emphases added)." *KSR*, 550 U.S. at ___, 82 USPQ2d at 1396 *quoting In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). The Patent Office's assertions with respect to "provid[ing] more dendritic cells in place of the autologous dendritic cells in order to obtain enough of the dendritic cell-tumor cell chimeric cells with which to treat the patient" does not satisfy this requirement as there has been no articulated basis for concluding that upon consideration of the Ohno reference, one of ordinary skill in the art would have been motivated to augment the number of APCs in the treatment at all, let alone with HLA-haploidentical APCs.

As such, applicants respectfully submit that it is only by using impermissible hindsight reasoning using applicants' own disclosure that the Patent Office can conclude that one of ordinary skill in the art would think to employ HLA-haploidentical APCs. As set

forth in M.P.E.P. § 2142, "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art" (emphasis added). Given that none of the references cited by the Patent Office mentions the use of HLA-haploidentical APCs, the only disclosure relating to this particular source of APCs is applicants' specification. Since applicants' specification cannot provide the motivation for combining references, applicants respectfully submit that the instant rejection is believed to be improperly based on hindsight.

Summarily, in the instant rejection, the Patent Office has provided no basis independent of applicants' disclosure for concluding that one of ordinary skill in the art would have been motivated to employ HLA-haploidentical APCs. Therefore, applicants respectfully submit that the instant rejection is not a case where the Patent Office has only taken into account knowledge asserted to be within the level of one of ordinary skill in the art at the time the claimed invention was made. Rather, the use of applicants' specification to provide the motivation to combine the references is improper, and thus the Patent Office has failed to establish a *prima facie* case of obviousness of claims 23, 27, 28, 30, 32-34, 37-40, and 43-46 over Ohno.

Accordingly, applicants respectfully submit that the instant obviousness rejection of 23, 27, 28, 30, 32-34, 37-40, and 43-46 over Ohno is believed to be improper, and respectfully request that it be withdrawn at this time. Applicants further respectfully submit that claims 23-30 and 32-46 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

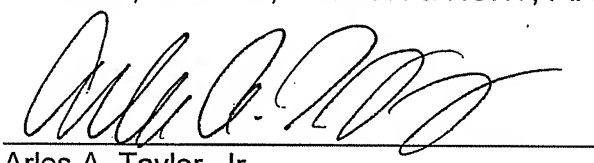
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any underpayment or credit any overpayment of fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: March 3, 2008 By: 

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